Attorney Docket: 2201/49996

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	ISAO SAKATA et al.		
Serial No.:	09/889,698	Group Art Unit:	1616
Filed:	July 20, 2001	Examiner:	Dameron Jones
Title:	Porphyrin Compounds		

DECLARATION UNDER 37 C.F.R. 1.132

I, YOSHINORI NAKAE, hereby declare that:

1. I am listed as an inventor in the above-referenced patent application and am familiar with the patent application and the claims therein, as well as the Sakata et al. reference (JP 09124652). I am also familiar with the porphyrin compounds and mixtures of porphyrin compounds described in these documents.

2. I conducted an experiment to compare the accumulability in cancerous tissues of the porphyrin compound claimed in the present application with that of the isomeric mixture porphyrin compound of the Sakata reference.

3. In particular, I examined the porphyrin compound of claim 9 of the present application, that is, 13,17-bis[(1,2-dicarboxyethyl) carbamoylethyl]-3-ethenyl-7-hydroxy-8-ethoxyiminoethylidene-2,7,12,18-tetramethyl-porphyrin ("Compound I") and the isomeric mixture of Compound I, that is, an isomeric mixture of 13,17-bis[(1,2-dicarboxyethyl)carbamoylethyl]-3-ethenyl-7-hydroxy-8-

thoxyiminoethylidene-2,7,12,18-tetramethyl-porphyrin, as described in the Sakata reference (the "Isomeric Mixture").

4. In order to compare the accumulability of the compounds, 3H/He mice (5 per group) were implanted with tumor tissues of colon cancer Colon 26 for 14 to 21 days, and were given an intravenous injection of sodium salt of each of Compound I and the Isomeric Mixture (10mg/kg for each mouse) which had been diluted with distilled water for injection.

5. After the injection, blood samples were collected from the mice and organs bearing the tumor tissue were extirpated and irradiated with an N_2-pulsed laser (N_2, wavelength: 337 nm, 2ns, 400-1000 nm). The excited fluorescent spectrum was measured. The wavelength in the range of 600 to 900 nm was examined based on the peak wavelength of NADH at 470 nm. Thus, the distribution of the test compound in the organ was determined by surface fluorescence using N_2 pulsed laser spectrophotometry. In this method, the distribution concentration of sodium salt of the test compound in a cancer/organ ratio was determined by calculating the peak wavelength at 670 nm when the peak wavelength at 470 nm was considered as the basic value, 1.

6. The results obtained 1 to 24 hours after administration of the compounds are shown in Figure 1 attached as Appendix A hereto.

7. Figure 1 shows the relative accumulability of Compound I and the Isomeric Mixture in cancerous tissues (by cancer/organ

concentration). The curv s represent the result of the average sum total values for cancer/brain, cancer/liver, and cancer/lung.

8. As clearly shown in Figure 1, Compound I (the claimed compound) has a significantly higher accumulability to cancerous tissues than does the Isomeric Mixture (the compound taught in the Sakata reference).

9. This significantly higher accumulability is an unexpected beneficial property of the claimed compound. This beneficial property of the claimed compound would not have been expected and could not have been predicted based on the Sakata reference.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent issued thereon.

11/18/'03
Date

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